



AM100788

SEQUENCE LISTING

<110> WYETH HOLDING CORPORATION.; KUNZ, ARTHUR ET AL.

<120> CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES

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<170> SeqWin99, version 1.02

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Gly

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Asp Val Val Val Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Phe Gly
 1 5 10 15

Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser
 20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr Cys Leu Gln Gly
 85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

Arg

<210> 8

<211> 121

<212> PRT

<213> mouse monoclonal 5/44 VH domain

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<223> mouse monoclonal 5/44 VH domain

<220>

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<400> 8

Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30

Trp Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 9
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<400> 9
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<400> 13
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Gly

<210> 14
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 <223> K60R

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<400> 14
 Gly Asn Asn Tyr Thr Thr Tyr Arg Arg Asn Leu Lys Gly
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<223> CDR-H2 (K60R)R H''

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<400> 15

Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Arg Arg Asn Leu Lys
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Gly

<210> 16

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<223> CDR-H2 (T57A K60R) H'''

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<400> 16

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Gly

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<211> 70

<212> PRT

<213> Homo sapien

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<223> DPK9

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<400> 17

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Asp Arg Val Thr Ile Thr Cys Trp Tyr Gln Gln Lys Pro Gly Lys Ala
 20 25 30

Pro Lys Leu Leu Ile Tyr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
 35 40 45

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
 50 55 60

Phe Ala Thr Tyr Tyr Cys
65 70

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<213> Homo sapiens

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<223> JK1

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<400> 18
Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
1 5 10

<210> 19
<211> 113
<212> PRT
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<223> gL1

<220>
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<400> 19
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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser
20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala
35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75 80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly
85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg

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 <223> gL2

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 Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser Leu Ala Asn Ser
 20 25 30
 Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
 65 70 75 80
 Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly
 85 90 95
 Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

Arg

<210> 21
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 <213> Homo sapiens

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 <223> DP7

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<400> 21
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Trp Val
 20 25 30
 Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Lys Phe Gln Gly
 35 40 45

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu
 50 55 60

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
 65 70 75 80

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 <223> JH4

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<400> 22
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<400> 23
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 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Gln Tyr Thr Thr Tyr Lys Arg Asn Leu
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

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<400> 24
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 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu
 50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

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 <212> PRT
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 <223> gH5

<220>
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<400> 25
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 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30
 Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu
 50 55 60
 Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

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 <212> PRT
 <213> Artificial Sequence

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 <223> gH6

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<400> 26
 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30
 Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe
 50 55 60
 Gln Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 27
 <211> 121
 <212> PRT
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 <223> gH7

<220>
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<400> 27
 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
 20 25 30
 Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 28
 <211> 239
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Full sequence of grafted light chain

<220>
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<400> 28
 Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Leu Phe Trp Ile Pro
 1 5 10 15
 Ala Ser Arg Gly Asp Val Gln Val Thr Gln Ser Pro Ser Ser Leu Ser
 20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser
 35 40 45
 Leu Ala Asn Ser Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys
 50 55 60
 Pro Gly Lys Ala Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
 65 70 75 80
 Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 85 90 95
 Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
 100 105 110
 Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys
 115 120 125
 Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
 130 135 140
 Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
 145 150 155 160
 Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
 165 170 175
 Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
 180 185 190
 Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
 195 200 205
 Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
 210 215 220
 Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 29
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Full sequence of grafted light chain

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<400> 29
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 ggagaccggg tcaccatcac ttgtagatcc agtcagagtc ttgcaaacag ttatgggaac 180

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gtctacgcct gcgaagtcac ccatcagggc ctgagctcgc ccgtcacaaa gagcttcaac 720
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<210> 30
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<212> PRT
<213> Artificial Sequence

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<220>
<223> Full sequence of grafted heavy chain

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<220>
<221>

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<400> 30
Met Asp Phe Gly Phe Ser Leu Val Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15
Val Gln Cys Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe
35 40 45
Thr Asn Tyr Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Ile Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg
65 70 75 80
Arg Lys Phe Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser
85 90 95
Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala
115 120 125
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140
Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
145 150 155 160
Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro

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165					170					175					
Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr
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Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val
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Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Lys	Thr	Tyr	Thr	Cys	Asn
	210					215					220				
Val	Asp	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Ser
225						230					235				240
Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Phe	Leu	Gly
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Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met
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Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly
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Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ser	Ser	Ile
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Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val
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Tyr	Thr	Leu	Pro	Pro	Ser	Gln	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val	Ser
	370					375					380				
Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu
385						390					395				400
Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro
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Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Arg	Leu	Thr	Val
			420					425					430		
Asp	Lys	Ser	Arg	Trp	Gln	Glu	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met
		435					440					445			
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Leu Gly Lys
465

<210> 31
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<212> DNA
<213> Artificial Sequence

<220>
<223> Full DNA sequence of grafted heavy chain

<220>
<221>

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<400> 31
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<212> DNA
 <213> Artificial Sequence

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 <223> 544gH1 T1

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<220>
 <223> 544gH1 T2

<220>
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<400> 33
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 <223> 544gH1 T3

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<400> 34
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 acagtctcct cagcttctac aaagggccca agaaa 95

<210> 35
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 <213> Artificial Sequence

<220>
 <223> 544 gH1 B1

<220>
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<400> 35

ggaccaattg cacctcacac tgcactccct tgagaatgag tgccaggaac acgagagaga 60
atccgaagtc catggtggcg gcaagctttt attc 94

<210> 36
<211> 97
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 B2

<220>
<221>

<400> 36
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aatgaatcca ataatttgtg aacctgtagc cgctagc 97

<210> 37
<211> 93
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1B3

<220>
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atgacagctc catgtagaca gtgcttgtgg agg 93

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<211> 21
<212> DNA
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<223> 544gH1 F1

<220>
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<400> 38
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<210> 39
<211> 22
<212> DNA
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<220>
<223> 544gH1 R1

<220>

<221>

<400> 39

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22

<210> 40

<211> 87

<212> DNA

<213> Artificial Sequence

<220>

<223> 544gL1 T1

<220>

<221>

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gcttcccggg gtgacgttca agtgaccag agcccatcca gcctgagcgc atctgtagga

60

gaccgggtca ccatcacttg tagatcc

87

<210> 41

<211> 90

<212> DNA

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<223> 544gL1 T2

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60

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90

<210> 42

<211> 91

<212> DNA

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<223> 544gL1 T3

<220>

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60

tactaaagta gaaatcaaac gtacggcgtg c

91

<210> 43

<211> 88

<212> DNA

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<223> 544gL1 B1

<220>

<221>

<400> 43

gaacgtcacc ccgggaagca ggaatccaga acaacagaag caccaacagc ctaacaggca 60
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<210> 44

<211> 88

<212> DNA

<213> Artificial Sequence

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<223> 544gL1 B2

<220>

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<212> DNA

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<223> 544gL1B3

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<212> DNA

<213> Artificial Sequence

<220>

<223> 544gL1 F1

<220>

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<400> 46

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<210> 47
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<220>
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<400> 47
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21

<210> 48
 <211> 339
 <212> DNA
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<220>
 <223> DNA sequence of mouse monoclonal 5/44 VL

<220>
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<400> 48
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 tacctgcaca agcctggcca gtctccacag ctctcatct atgggatttc caacagattt 180
 tctgggggtgc cagacagggt cactggcagt gggttcaggga cagatttcac actcaagatc 240
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 tacacgttcg gaggggggac caagctggaa ataaaacgt 339

<210> 49
 <211> 363
 <212> DNA
 <213> mouse

<220>
 <223> DNA sequence of mouse monoclonal 5/44 VH

<220>
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<400> 49
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 cctgggcagg gtctagaatg gattgggtgtg attaatcctg gaaataatta tactacgtat 180
 aagaggaact tgaagggcaa ggccacactg actgcagtca catccgccag cactgcctac 240
 atggacctca gcagcctgac aagtgaggac tctgcgggtc attactgtac aagagagggc 300
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 tca 363

<210> 50
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<212> DNA
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<220>
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<400> 50
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<210> 51
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 <212> DNA
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<220>
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<400> 51
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 ctcaagggag tgcagtgtga ggtgcagctc gtcgagtctg g 101

<210> 52
 <211> 110
 <212> DNA
 <213> Artificial

<220>
 <223> gH4 oligonucleotide

<400> 52
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 tattgatgcg atgtatatcc tctttagatt tcccgtctcg ttgcgactgg 110

<210> 53
 <211> 20
 <212> PRT
 <213> Artificial

<220>
 <223> gH4 graft

<400> 53

Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu Lys Gly Arg Ala
 1 5 10 15

Thr Leu Thr Ala
 20

<210> 54

<211> 110
 <212> DNA
 <213> Artificial

<220>
 <223> gH5 oligonucleotide

<400> 54
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<210> 55
 <211> 20
 <212> PRT
 <213> Artificial

<220>
 <223> gH5 graft

<400> 55

Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe Gln Gly Arg Val
 1 5 10 15

Thr Met Thr Ala
 20

<210> 56
 <211> 110
 <212> DNA
 <213> Artificial

<220>
 <223> gH6 oligonucleotide

<400> 56
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<210> 57
 <211> 20
 <212> PRT
 <213> Artificial

<220>
 <223> gH6 graft

<400> 57

Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe Gln Gly Arg Ala
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Thr Leu Thr Ala
 20

<210> 58
 <211> 110
 <212> DNA
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<220>
 <223> gH7 oligonucleotide

<400> 58
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 tattgatgcg atgtatatcc tcttttaagg tcccgtctca atgctactgg 110

<210> 59
 <211> 20
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 <213> Artificial

<220>
 <223> gH7 graft

<400> 59

Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe Gln Gly Arg Val
 1 5 10 15

Thr Met Thr Ala
 20

<210> 60
 <211> 123
 <212> DNA
 <213> Artificial

<220>
 <223> gL2 oligonucleotide

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 gccactgcaa cagcactggg tctcgggtag gtcggactcg cgtagacatc ctctggccca 120
 gtg 123

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 <212> PRT
 <213> Artificial

<220>
 <223> gL2 graft

<400> 61

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Ser	Val	Gly	Asp	Arg	Val	Thr
			20			